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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/402,273 | 12/13/1999 | JORJ TERRY ULRICH | 9950-0002 | 5731 |

7590 12/18/2001

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| EXAMINER | |
|---|---|
| HUYNH, PHUONG N | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

DATE MAILED: 12/18/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/402,273 | ULRICH ET AL. | |
| | Examiner | Art Unit | |
| | " Neon" Phuong Huynh | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 October 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

**DETAILED ACTION**

1. Claims 1-2 and 6-8 are pending.

2. In view of the amendment filed 10/9/01, only the following rejections remain.

3. Claims 1-2 and 6-8 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had position of the claimed invention for the same reasons set forth in Paper No 9.

Applicants' arguments filed 10/9/01 have been fully considered but are not found persuasive. Applicants' position is that (1) as stated in the Interim Guidelines, "[w]what is conventional or well known to one skilled in the art need not be disclosed in detail, (2) the term "optionally modified allergen" is conventional and (3) the term is commonly understood genus.

However, the term "modified allergen" encompasses amino acid substitution, deletion, and chemical modification such as intra-molecular cross-linking of allergen by glutaraldehyde. The specification as filed discloses only one modified allergen, that is, glutaraldehyde modified ovalbumin (See page 4 of the specification). Furthermore, the term "optionally" implies that allergen needs not be modified. The specification as filed requires that the allergen be chemically modified (See page 4 of the specification). Given the indefinite number of "optionally modified allergen", the specification does not reasonably provide a **written description** of any pharmaceutical composition capable of selectively enhancing TH1 response comprising any "optionally modified allergen". With the exception of the glutaraldehyde modified ovalbumin, there is no additional species of (1) modified allergen and (2) unmodified allergen for a pharmaceutical composition for enhancing TH1 immune response. Given the lack of a written description of *any* "optionally modified allergen" and any additional representative species of "modified allergen" as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

4. Claims 1-2 and 6-8 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising an allergen modified by intra-molecular cross-linking to reduce allergenicity or comprising a polymerized allergen, does not reasonably provide enablement for making and/or using the claimed "optionally modified allergen" for the same reasons set forth in Paper No 9.

Applicants' arguments filed 10/9/01 have been fully considered but are not found persuasive. Applicants' position is that the term "modified allergen" is a term well known in the field and encompasses all manner of crosslinked and polymerized allergens".

However, the term "modified allergen" encompasses amino acid substitution, deletion of as well as chemical modification such as intra-molecular cross-linking of allergen by glutaraldehyde. The specification as filed discloses only one modified allergen, that is, glutaraldehyde modified ovalbumin (See page 4 of the specification). Furthermore, the term "optionally" implies that allergen needs not be modified. The specification as filed requires that the allergen be chemically modified (See page 4 of the specification). Given the indefinite number of undisclosed "modified allergen", the insufficient guidance and working examples in the specification as filed, it is unpredictable which undisclosed modified allergen would be useful for a pharmaceutical composition that is capable of enhancing TH1 immune response. For these reasons, the specification as filed fails to enable one skill in the art to practice the invention without undue amount of experimentation. As such, further research would be required to practice the claimed invention.

5. Claims 1-2 and 6-8 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the same reasons set forth in Paper No 9.

Applicants' arguments filed 10/9/01 have been fully considered but are not found persuasive. Applicants' position is that the term "optionally modified allergen" as recited in claim 1 is well known and understood in the art.

However, the recitation of "optionally modified allergen" in claim 1 and dependent claims is ambiguous and indefinite. The specification on page 4 requires that be modified with glutaraldehyde and modification is not an option.

6. Claims 1-2 and 6-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/34626 (PTO 1449) in view of WO 92/16556 (PTO 1449) and US Pat No. 5,795,862 for the same reasons set forth in Paper No 9.

Applicants' arguments filed 10/9/01 have been fully considered but are not found persuasive. Applicants' position is that amended claim 1 recites a pharmaceutical composition capable of selectively enhancing TH1 response; (2) Van Wijnendale et al (WO 92/16556) teach that in the context of the prophylactic and therapeutic treatment of HIV infections, 3-DMPL is able to stimulate both arms (i.e., the neutralizing antibody and the effector cell-mediated immunity of the immune system; (3) Van Wijnendale et al do not teach or suggest that 3-DMPL is suitable for use in allergen formulation; (4) the '862 patent does not teach or suggest the inclusion of 3-DMPL; (5) the second criterion for prima facie obviousness has not been met.

However, the WO/9634626 publication teaches a pharmaceutical composition comprising tyrosine and modified allergen such as glutaraldehyde polymerized D. pternyssinus extract protein, ragweed or birch pollen allergen for use in desensitization therapy of allergy sufferers (See entire document, page 1 lines 17-18 and claims of WO96/34626, in particular).

The claimed invention differs from the reference only by the recitation of said composition comprises 3-DMPL and capable of selectively enhancing TH1 response.

The WO 92/16556 publication (Van Wijnendale et al) teaches a pharmaceutical composition comprising an unmodified antigen such as gp160 or modified antigen such as derivative of gp160 and 3 Deacylated monophosphoryl lipid A which is 3D-Mpl as an adjuvant for stimulating antigen specific neutralizing antibody and cell mediated immunity (Delayed type hypersensitivity, DTH) by injection (See page 22, example 2a, pages 24-25, pages 28-29 claim 9 of WO 92/16556, in particular). The WO 92/16556 publication further teaches that the adjuvant formulations containing 3D MPL are able to induce a specific T cell response and improve humoral and effector cell mediated (DTH) immune response wherein the DTH immune response is a TH1 response (See page 29, lines 8-16, in particular).

The '862 patent teaches a therapeutic composition for use in desensitization therapy comprising at least one isolated allergen such as flea saliva protein and further comprising an

adjuvant and a carrier (See claims 22 and 25 of '862 patent, column 4, lines 19-21 and 30-33, sentence spanning from column 7 bridging column 8, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to combine the 3-DMPL adjuvant as taught by the WO 92/16556 publication in a pharmaceutical composition comprising tyrosine and modified allergen for desensitization therapy as taught by the WO/9634626 publication and unmodified allergen in a pharmaceutical composition for use in desensitization therapy as taught by the '862 patent. From the combined teachings of the references at the time the invention was made, one would have had a reasonable expectation of success in producing the claimed invention

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the WO 92/16556 publication teaches that the adjuvant formulations containing 3D MPL are able to induce a specific T cell response and improve humoral and effector cell mediated (DTH) immune response that is a TH1 response (See page 29, lines 8-16, in particular). The WO/9634626 publication teaches that a pharmaceutical composition comprising tyrosine and modified allergen such as glutaraldehyde polymerized allergen is useful for desensitization therapy of allergy sufferers since glutaraldehyde modified allergen reduces the antigenicity of said allergen and tyrosine coprecipitated with the modified allergen (See entire document, page 1, lines 6-10, page 1, line 17-18 and claims of WO96/34626, in particular). The '862 patent teaches that isolated unmodified allergen such as flea saliva protein and further comprising an adjuvant and a carrier is useful in desensitization therapy (See claims 22 and 25 of '862 patent, column 4, lines 19-21 and 30-33, sentence spanning from column 7 bridging column 8, in particular).

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
December 17, 2001

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